Biology of Microorganisms

Sixth Edition

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Chapter 12

Immunology and Immunity

Higher animals possess a highly sophisticated mechanism, the **immune response**, for developing resistance to specific microorganisms or viruses. The immunological response occurs because the body has a general system for the neutralization of foreign macromolecules and microbial cells. Foreign substances which elicit the immune response are called **antigens**. As a result of antigen stimulation, the immune system produces specific proteins called **antibodies** or **immunoglobulins** and specific cells called **activated T cells**. Since an invading microorganism contains a variety of macromolecules foreign to the host, antibodies and activated T cells are generated against it and are able to recognize the foreign material and bring about its destruction.

The immune response shows three major characteristics: *specificity, memory,* and *tolerance.* (1) The **specificity** of the antigen-antibody or antigen-T cell interaction is unlike any of the host-resistance mechanisms described in Chapter 11. Phagocytosis, inflammation, and the other nonspecific host resistance mechanisms develop against virtually any invading microorganism, even those the host has never encountered before, whereas in the immune response, a specific interaction must occur for *each* new invader. (2) Once the immune system produces a specific type of antibody or activated T cell, it is capable of producing more of the same antibody or T cell more rapidly and in larger amounts. This capacity for **memory** is of major importance in resistance of the host to subsequent reinfection or in the protection to the host provided by vaccination. (3) **Tolerance** exists because macromolecules on the surfaces of body cells are also potentially antigenic and would be damaged if antibodies and activated T cells to these body cells were produced during an immune response.

Immunity based on antibodies is called **humoral immunity** and immunity based on activated T cells is called **cellular immunity**. Figure 12.1 gives an overview of the immune response and contrasts the activities of humoral and cellular immunity. We shall discuss first the nature and formation of antibodies, and then show how they confer specific resistance to infection. Later, we will discuss the concepts of cellular immunity.

Several features of the immune response will be listed here and then discussed in some detail below.

1. Many but not all foreign macromolecules elicit the immunological response; those that do are called **immunogens.**
2. In virtually every case, an immune response directed against a foreign macromolecule occurs only if the animal is *challenged* with the foreign substance.
3. There is a high specificity in the immune response; antibodies or activated T cells made against one antigen generally do not react against other antigens.
4. Not all immune reactions are beneficial; some, such as those involved in hypersensitivities and autoimmune reactions, are harmful.
5. Antibodies are formed against a variety of foreign macromolecules, but ordinarily not against macromolecules of the animal's own tissues; thus the animal is able to distinguish between its own ("self") and foreign ("nonself") macromolecules.
6. Microorganisms and viruses that invade the host contain large numbers of different macromolecules that can act as antigens. Thus the immunological response can be made the basis of specific immunization procedures for the prevention and control of specific diseases.

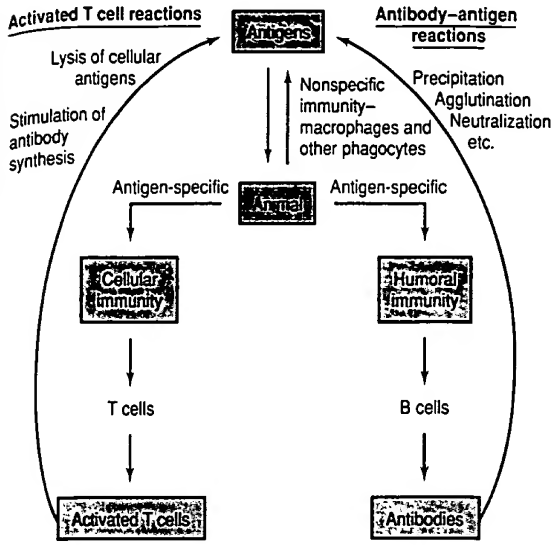

Figure 12.1 An overview of the immune response.

7. The high specificity of antigen-antibody reactions makes them useful in many research and diagnostic procedures.

The immune response is a specific reaction by the body to the presence of foreign material, generally macromolecules. The substance which induces the immune response is called an antigen or immunogen. As a result of antigenic stimulation, proteins called antibodies or immunoglobulins are produced, and specific cells called activated T cells are formed. Microorganisms and viruses capable of invading the body contain numerous antigens and the immune response participates in the prevention and control of infectious disease.

12.1 Immunogens and Antigens

Immunogens are substances that, when administered to an animal in the appropriate manner, induce an immune response. The immune response may involve either antibody production, the activation of specific immunologically-competent cells (called *activated T cells*), or both. **Antigens** are substances that react with either antibodies or activated T cells and most antigens are also immunogens. However, some substances are recognized by immune systems while not being true immunogens. For example, **haptens** are low-molecular weight substances that combine with specific antibody molecules but do not by themselves induce antibody formation. Haptens include such molecules as sugars, amino acids, and small polymers.

An enormous variety of macromolecules can act as immunogens under appropriate conditions. These include virtually all proteins and lipoproteins, many polysaccharides, some nucleic acids, and certain of the teichoic acids. One important requirement is that the molecules must be of fairly *high* molecular weight, usually greater than 10,000. However, the antibody is directed not against the antigenic macromolecule as a whole, but only against distinct portions of the molecule that are called its **antigenic determinants** (Figure 12.2). Chemically, antigenic determinants include sugars, amino acid side chains, organic acids and bases, hydrocarbons, and aromatic groups. Antibodies are formed most readily to determinants that project from the foreign molecule or to terminal residues of a polymer chain. In proteins, for example, the majority of antibodies are made to surface determinants, because the surface contains a continuum of antigenic sites. A region of as few as 4–5 amino acids can define an antigenic determinant on a protein. Also, the surface of a protein can and frequently will have many overlapping antigenic determinants. A cell or virus is a mosaic of proteins, polysaccharides, and other macromolecules, each of which is a potential antigen. Each antigen of the cell is also a mosaic of side chains and residues, each of which is a potential antigenic determinant. The immunological response to an invading microbe or virus is thus a complex phenomenon.

In general, the specificity of antibodies is comparable to that of enzymes, which are able to distinguish between closely related substances. For instance, antibodies can distinguish between the sugars glucose and galactose, which differ only in the position of the hydroxyl group on carbon 4. However, specificity is not absolute, and an antibody will react at least to some extent with determinants related to the one that induced its formation. The antigen which induced the antibody is called the **homologous antigen** and others, if any, that react with the antibody are called **heterologous antigens.**

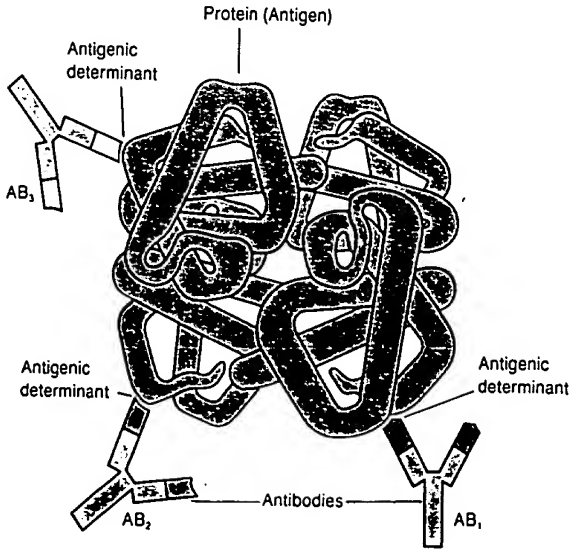

Figure 12.2 Antigens and antigenic determinants. Antigens may contain several different antigenic determinants, each capable of reacting with a specific antibody.

An immunogen is a substance that induces an immune response; if the immunogen reacts with either antibody or activated T cell it is called an antigen. Although the reaction between antigen and antibody or activated T cell is highly specific, it is not directed at the antigen as a whole, but just against one or more restricted portions of the antigen called its antigenic determinants. Although the specificity of the immune response is comparable to the specificity of enzyme and substrate, antibodies or activated T cells can sometimes react with heterologous antigens.

12.2 Immunoglobulins (Antibodies)

Immunoglobulins (antibodies) are protein molecules that are able to combine with antigenic determinants. They are found predominantly in the serum fraction of the blood, although they may also be found in other body fluids, as well as in milk. Serum is the fluid portion of the blood that is left when the blood cells and the materials responsible for clotting (fibrin, platelets, and various cofactors, see Section 11.13) are removed. Serum containing antibody is often called **antiserum**. Immunoglobulins (abbreviated Ig) can be separated into five major classes on the basis of their physical, chemical, and immunological properties: **IgG, IgA, IgM, IgD,** and **IgE** (Table 12.1). Immunoglobulin class IgG has been further resolved into four immunologically distinct subclasses called IgG_1, IgG_2, IgG_3, and IgG_4. The basis for this separation will be discussed below. Antibody molecules specific for a given antigenic determinant can be found in each of the several classes, even in a single immunized individual. Upon initial immunization, the first immunoglobulin to appear is IgM, a pentameric immunoglobulin with a molecular weight of about 970,000; IgG appears later. In most individuals about 80 percent of the immunoglobulins are IgG proteins, and these have therefore been studied most extensively.

Immunoglobulin structure

Immunoglobulin G is the most common circulating antibody and thus we will discuss its structure in some detail. Immunoglobulin G has a molecular weight of about 160,000 and is composed of four polypeptide chains (Figure 12.3). Both intrachain and interchain disulfide (S—S) bridges are present (Figure 12.3). The two light (short) chains are identical in amino acid sequence, as are the two heavy (longer) chains. The molecule as a whole is thus symmetrical (Figure 12.3). Each light chain consists of about 212 amino acids and each heavy chain consists of about 450 amino acids.

Table 12.1 Properties of human immunoglobulins

Class designation	Molecular weight	Proportion of total antibody (percent)	Concentration in serum (mg/ml)	Antigen binding sites	Properties	Distribution
IgA	160,000 385,000 (secretory form)	13	3 0.05	2 4	Major secretory antibody	Secretions (saliva, colostrum, serum), cellular and blood fluids; exists as a monomer in serum and as a dimer in secretions
IgG	146,000	80	13	2	Major circulating antibody; four subclasses exist: IgG_1, IgG_2, IgG_3, IgG_4; binds complement weakly; antitoxin	Extracellular fluid; blood and lymph; crosses placenta
IgM	970,000 (pentamer)	6	1.5	10	First antibody to appear after immunization; binds complement strongly	Blood and lymph; B lymphocyte surfaces (as monomer)
IgD	184,000	1	0.03	2	Minor circulating antibody; heat labile; high carbohydrate content	Blood and lymph; lymphocyte surfaces
IgE	188,000	0.002	0.00005	2	Involved in allergic reactions: contains mast cell binding fragment	Blood and lymph only